Retrovirology

Poster presentation

HIV-1 Glycopeptides as Immunogens

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One challenge in HIV-1 vaccine design is to identify epitopes able to induce neutralizing antibodies. HIV-1 glycopeptides represent a partial structure of the envelope glycoproteins that contains both peptide and carbohydrate motifs. Several pieces of evidence suggest that HIV-1 glycopeptides may constitute new neutralizing epitopes: 1) certain HIV-1 glycopeptides are highly conserved and are well accessible; 2) selected N-glycans around the V3 domain have been identified as neutralizing epitope for the broadly neutralizing antibody 2G12; and 3) N-glycans can mask unwanted epitopes, redirect the immune focus, and induce conformational epitopes. To explore this new territory for immunogen design, we have focused on exploring the V3 domain glycopeptides that correspond to the so-called principal neutralizing determinant (PND) and the gp41 C-terminal glycopeptides that are involved in viral membrane fusion. We have developed a novel chemoenzymatic method for constructing large homogeneous HIV-1 glycopeptides that are hitherto unavailable. Preliminary studies indicated that glycosylation affects the global conformations and enhances the beta-turn and/or loop structure of the V3 domain in buffer. We also observed that the N-glycans can protect the V3 domain against protease (furin and pronase) digestion. In addition, we found that glycosylation on C34 has a profound effect on its ability to form the six-helix bundles with N36. The interesting glycosylation effects observed urge further immunization studies with the glycopeptide immunogens.